



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,078	04/28/2005	Shunsuke Ishii	P27813	2400
7055 7590 01/09/2009 GREENBLUM & BERNSTEIN, P.L.C. 1950 ROLAND CLARKE PLACE RESTON, VA 20191				
EXAMINER EPFS FORD, JANET L				
ART UNIT		PAPER NUMBER		
1633				
NOTIFICATION DATE		DELIVERY MODE		
01/09/2009		ELECTRONIC		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com

pto@gbpatent.com

Office Action Summary

Application No.

10/533,078

Applicant(s)

ISHII ET AL.

Examiner

Janet L. Epps-Smith

Art Unit

1633

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 6, 8-12 and 25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6, 8-12 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SI-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Claims 13-24 were cancelled by Applicants.
3. Claims 1-4, 6, 8-12 and 25 are therefore currently under examination.

Response to Arguments

Claim Rejections - 35 USC § 102

4. The rejection of claims 1-4 and 25 under 35 U.S.C. 102(b) as being anticipated by Xia et al. (published online September 16, 2002), is withdrawn in response to Applicant's amendment.

Claim Rejections - 35 USC § 103

5. Applicant's arguments with respect to claims 1-8, 10-12 and 25 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-4, 6, 8, 10-12, and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xia et al. in view of Huang et al., Perkins et al. (US 2003/0119104 A1) and Yonaha et al.; and further in view of Nomura et al. and GenBank accession No AF435852.

8. Xia et al. discloses a construct that expresses an siRNA of 21 base pairs that forms a hairpin structure, wherein the hairpin comprises a sequence that is complementary to enhanced green fluorescent protein. The hairpin was placed under the control of the CMV promoter and comprised a poly(A) cassette. This disclosure meets the limitations of instant claims 1-4. Xia et al. also teach transfection of these constructs into mammalian cells, particularly HEK-293 cells(see page 1006). This disclosure reads on the limitations of instant claim 25.

9. Xia et al. discloses constructs encoding a hairpin structure under the control of RNA polymerase II. However, Xia et al. does not teach (1) constructs comprising a pause site; (2) Xia et al. does not disclose a construct for the expression of a hairpin and a ribozyme; (3) Xia et al. does not teach constructs targeting the *ski* gene.

(1) Perkins et al. teach recombinant vectors comprising with the following elements: immediate/early human CMV enhancer/promoter with intron A, multiple cloning sites, a pause site from the human alpha 2 globin gene, see paragraph [0316], and a polyA SV40 terminator sequence (see paragraph [0317]). Perkins et al. also teach that the constructs of their invention can be used to express siRNA, and that the siRNA encoding sequences can be placed under the control or regulation of a regulatable or inducible promoter that would allow one to temporally and/or spatially control the knockdown effect of the corresponding gene, see paragraph [0077].

(1) Additionally, Yonaha et al. discloses the use of MAZ sequences as pause sites that function to both pause Pol II transcription and activate polyadenylation.

(2) Huang et al. discloses a construct for the production of a transcription product comprising a stem-loop (or hairpin) structure and a ribozyme.

(3) Nomura et al. describes the *ski* gene as a proto-oncogene, moreover this reference teaches that overexpression of this gene results in the oncogenic transformation of embryonic fibroblast. Moreover, Nomura et al. teach that overexpression of the *ski* gene in transgenic mice results in hypertrophic growth. The sequence of the mouse *ski* gene is disclosed in the prior art as GenBank Accession No. AF43582.

10. (1) It would have been obvious to the ordinary skilled artisan at the time of the instant invention to modify the constructs of Xia et al. with the teachings of Perkins et al. in the design of the instant invention. One of ordinary skill in the art would have been motivated to modify the teachings of Xia et al. with the construct elements of Perkins et al. since the constructs of Perkins et al. are disclosed for the same purpose as the constructs of Xia et al., namely for the efficient expression of nucleic acid, including siRNA, in mammalian cells.

11. Absent evidence of the unexpected results, the ordinary skilled artisan would expected to have had a high degree of success in designing constructs for the expression of siRNA following the teachings according to Xia et al. in view of Perkins et al. since both references provide sufficient guidance in designing constructs for the expression of siRNA. Moreover, since Yonaha et al. presents the MAZ domain, it cannot be considered to be especially difficult to substitute the MAZ domain into the constructs of Xia et al. and Perkins et al. for the activation of polyadenylation.

12. (2) Moreover, it would have been obvious to the ordinary skilled artisan to modify the constructs of Xia et al. with the ribozyme constructs of Huang et al. to comprise the expression of both a hairpin and ribozyme. The ribozyme constructs of Huang et al. were designed to control the polyadenylation of the transcript product, and thereby regulate the nuclear export of the transcript. The ordinary skilled artisan seeking to design alternative constructs for expressing hairpin comprising transcripts would have been motivated to design the constructs according to the present invention since the addition of the autocatalytically cleavable ribozyme would enhance the functionality of the transcript produced by the prior art constructs.

13. (3) It would have been obvious to the ordinary skilled artisan to modify the teachings of Xia et al. with the teachings of Nomura et al. and GenBank Accession No. AF43582 in the design of the instant invention. Absent evidence to the contrary the ordinary skilled artisan would have been motivated and would have had a reasonable expectation for success in designing dsRNA constructs according to Xia et al. targeting the *ski* gene, since the prior art describes the dsRNA constructs as useful for targeting any given gene, and the prior art discloses the *ski* gene as a disease-related gene. Moreover, since a sequence encoding a *ski* gene was disclosed in the GenBank database, it would have been a simple task for the ordinary skilled artisan to design a dsRNA construct targeting this sequence.

Claim Rejections - 35 USC § 112

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 6 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. The rejection of claim 5 under this statute set forth in the prior Office Action is withdrawn since Applicants cancelled this claim.

17. Applicants have amended claim 6, however the claim still recites "wherein the sequence that autocatalytically cleaves RNA is a ribozyme site." It remains that this statement is unclear since a site that is cleaved by a ribozyme, e.g. an NUX site, does not have the ability to cleave RNA, it is a site that is recognized by the ribozyme, not the ribozyme itself.

18. Claims 1-4, 6, 8-12 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. Claim 1 and those claims dependent therefrom recite, at line (a-1) "the target gene," there is insufficient antecedent basis for this limitation in the claim. Moreover, Applicants have added part (d) to the claim. Part (d) refers to a sequence that autocatalytically cleaves RNA located upstream of these sequences. It is assumed that part (a)-(c) read on DNA sequences that must be transcribed into RNA, see the last

three lines of the claim. There is no RNA located upstream of nucleotide sequences (a) to (c).

20. The rejection of claims 1-12 and 25 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's arguments.

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE